Claims

1. A method for producing a secreted, biologically active dimerized polypeptide fusion, comprising:

introducing into a eukaryotic host cell a DNA construct comprising a transcriptional promoter operatively linked to a secretory signal sequence followed downstream by and in proper reading frame with a DNA sequence encoding a non-immunoglobulin polypeptide requiring dimerization for biological activity joined to a dimerizing protein;

growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a dimerized polypeptide fusion encoded by said DNA sequence; and

isolating said dimerized polypeptide fusion from said host cell.

2. A method for producing a secreted, biologically active dimerized polypeptide fusion, comprising:

introducing into a eukaryotic host cell a first DNA construct comprising a transcriptional promoter operatively linked to a first secretory signal sequence followed downstream by and in proper reading frame with a first DNA sequence encoding a non-immunoglobulin polypeptide requiring dimerization for biological activity joined to an immunoglobulin light chain constant region;

introducing into said host cell a second DNA construct comprising a transcriptional promoter operatively linked to a second secretory signal sequence followed downstream by and in proper reading frame with a second DNA sequence encoding an immunoglobulin heavy chain constant region domain selected from the group consisting of C_H1, C_H2, C_H3, and C_H4;

growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a biologically active dimerized polypeptide fusion encoded by said first and second DNA sequences; and

isolating said biologically active dimerized polypeptide fusion from said host cell.

3. The method of claim 2 wherein said second DNA sequence further encodes an immunoglobulin hinge region and wherein said hinge region is joined to said immunoglobulin heavy chain constant region.

4. The method of claim 2 wherein said second DNA sequence further encodes an immunoglobulin variable region and wherein said variable region is joined upstream of and in proper reading frame with said immunoglobulin heavy chain constant region domain.

5. The method of claim 2 wherein said host cell is a fungal cell or a cultured mammalian cell.

6. The method of claim 2 wherein said host cell is a cultured rodent myeloma cell line.

7. The method of claim 2 wherein said non-immunoglobulin polypeptide requiring dimerization for biological activity is selected from the group consisting of a polypeptide comprising the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine, number 29, to lysine, number 531, a polypeptide comprising the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine, number 29, to methionine, number 441, and a polypeptide comprising the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524.

8. A method for producing a secreted, biologically active dimerized polypeptide fusion, comprising:

introducing into a eukaryotic host cell a first DNA construct comprising a transcriptional promoter operatively linked to a first secretory signal sequence followed

downstream by and in proper reading frame with a first DNA sequence encoding a non-immunoglobulin polypeptide requiring dimerization for biological activity joined to an immunoglobulin heavy chain constant region domain selected from the group consisting of C_H1, C_H2, C_H3, and C_H4;

introducing into said host cell a second DNA construct comprising a transcriptional promoter operatively linked to a second secretory signal sequence followed downstream by and in proper reading frame with a second DNA sequence encoding an immunoglobulin light chain constant region;

growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a biologically active dimerized polypeptide fusion encoded by said first and second DNA sequences; and

isolating said biologically acitve dimerized polypeptide fusion from said host cell.

9. The method of claim 8 wherein said first DNA sequence further encodes an immunoglobulin hinge region and wherein said hinge region is joined to said immunoglobulin constant region.

10. The method of claim 8 wherein said second DNA sequence further encodes an immunoglobulin variable region and wherein said variable region is joined upstream of and in proper reading frame with said immunoglobulin light chain constant region domain.

11. The method of claim 8 wherein said host cell is a fungal cell or a cultured mammalian cell.

12. The method of claim 8 wherein said host cell is a cultured rodent myeloma cell line.

13. The method of claim 8 wherein said non-immunoglobulin polypeptide requiring dimerization for

biological activity is selected from the group consisting of a polypeptide comprising the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine, number 29, to lysine, number 531 a polypeptide comprising the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2)from isoleucine, number 29, to methionine, number 441, and a polypeptide comprising the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524.

14. A method for producing a secreted receptor analog, comprising:

introducing into a eukaryotic host cell a DNA construct comprising a transcriptional promoter operatively linked to at least one secretory signal sequence followed downstream by and in proper reading frame with a DNA sequence encoding a ligand-binding domain of a receptor requiring dimerization for biological activity joined to a dimerizing protein;

growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a receptor analog encoded by said DNA sequence; and

isolating said receptor analog from said host cell.

15. A method for determining the presence of PDGF or isoforms thereof in a biological sample, comprising:

incubating a polypeptide comprising a PDGF receptor analog fused to a dimerizing protein with a biological sample suspected of comprising PDGF or an isoform thereof under physiological conditions to allow the formation of receptor/ligand complexes; and

detecting the presence of the receptor/ligand complexes as an indication of the presence of human PDGF or an isoform thereof.

16. The method of claim 15 wherein the polypeptide is tagged with a label selected from the group consisting of radionuclides, fluorophores, enzymes, and luminescers.

17. The method of claim 15 wherein the biological sample is selected from the group consisting of blood, urine, plasma, serum, platelet and other cell lysates, platelet releasates, cell suspensions, cell-conditioned culture media and chemically or physically separated portions thereof.

18. The method of claim 15 wherein said human PDGF receptor analog is selected from the group consisting of the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine, number 29, to methionine, number 441, joined to a dimerizing protein, the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine, number 29, to lysine, number 531, joined to a dimerizing protein and the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524, joined to a dimerizing protein.

19. The method of claim 15 wherein said dimerizing protein comprises at least a portion of a protein selected from the group consisting of an immunoglobulin light chain, an immunoglobulin heavy chain and yeast invertase, wherein said portion associates as a dimer in a covalent or a noncovalent manner.

20. A method for producing a secreted PDGF receptor analog, comprising:

introducing into a eukaryotic host cell a DNA construct comprising a transcriptional promoter operatively linked to a secretory signal sequence followed downstream in proper reading frame by a DNA sequence encoding a ligand-binding domain of a PDGF receptor;

growing said host cell in an appropriate growth medium under physiological conditions to allow the secretion of a PDGF receptor analog encoded by said DNA sequence; and

isolating said PDGF receptor analog from said host cell.

21. A method for producing a secreted PDGF receptor analog, comprising:

introducing into a cultured rodent myeloma cell a DNA construct comprising a transcriptional promoter operatively linked to a PDGF receptor signal sequence followed downstream by and in proper reading frame with a DNA sequence encoding the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24, to glutamic acid, number 524, joined to a dimerizing protein, wherein said dimerizing protein is an immunoglobulin constant region selected from the group consisting of C_H1, C_H2, C_H3, C_H4 and C_κ joined to an immunoglobulint hinge region;

growing said cultured rodent myeloma cell in an appropriate growth medium under physiological conditions to allow the secretion of a PDGF receptor analog encoded by said DNA sequence; and

isolating the PDGF receptor analog from said cultured rodent myeloma cell.

22. A method for producing a secreted PDGF receptor analog, comprising:

introducing into a cultured rodent myeloma cell a first DNA construct comprising a transcriptional promoter operatively linked to a PDGF receptor signal sequence followed downstream by and in proper reading frame with a first DNA sequence encoding the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine, number 29, to lysine, number 531 joined to an immunoglobulin light chain constant region;

introducing into said cultured rodent myeloma cell a second DNA construct comprising a transcriptional promoter

operatively linked to a PDGF receptor signal sequence followed downstream by and in proper reading frame with a second DNA sequence encoding the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine number 29, to lysine, number 531 joined to an immunoglobulin heavy chain constant region domain selected from the group consisting of C_H1, C_H2, C_H3, and C_H4 joined to an immunoglobulin hinge region;

growing said cultured rodent myeloma cell in an appropriate growth medium under physiological conditions to allow the secretion of a PDGF receptor analog encoded by said first and second DNA sequences; and

isolating said PDGF receptor analog from said cultured rodent myeloma cell.

23. A method for producing a secreted PDGF receptor analog, comprising:

introducing into a cultured rodent myeloma cell a first DNA construct comprising a mouse V_H promoter operatively linked to a PDGF receptor signal sequence followed downstream of and in proper reading frame with a DNA sequence encoding the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524, joined to an immunoglobulin heavy chain constant region domain selected from the group consisting of C_H1, C_H2, C_H3 and C_H4 joined to an immunoglobulin hinge region;

introducing into said cultured rodent myeloma cell a second DNA construct comprising a mouse V_K promoter operatively linked to a PDGF receptor signal sequence followed downstream of and in proper reading frame with a DNA sequence encoding the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524, joined to an immunoglobulin light chain constant region;

growing said cultured rodent myeloma cell in an appropriate growth medium under physiological conditions to

allow the secretion of a PDGF receptor analog encoded by said first and second DNA sequences; and

isolating said PDGF receptor analog from said cultured myeloma cell.

24. A method for producing a secreted PDGF receptor analog, comprising:

introducing into a cultured rodent myeloma cell a first DNA construct comprising a mouse V_H promoter operatively linked to a PDGF receptor signal sequence followed downstream of and in proper reading frame with a DNA sequence encoding the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine number 29, to lysine, number 531, joined to an immunoglobulin heavy chain constant region domain selected from the group consisting of C_H1, C_H2, C_H3 and C_H4 joined to an immunoglobulin hinge region;

introducing into said cultured rodent myeloma cell a second DNA construct comprising a mouse V_K promoter operatively linked to a PDGF receptor signal sequence followed downstream of and in proper reading frame with a DNA sequence encoding the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524, joined to an immunoglobulin light chain constant region;

growing said cultured rodent myeloma cell in an appropriate growth medium under physiological conditions to allow the secretion of a PDGF receptor analog encoded by said first and second DNA sequences; and

isolating said PDGF receptor analog from said cultured myeloma cell.

25. A method for producing a secreted PDGF receptor analog, comprising:

introducing into a cultured rodent myeloma cell a first DNA construct comprising a mouse V_H promoter operatively linked to a PDGF receptor signal sequence followed downstream of and in proper reading frame with a DNA sequence encoding

the amino acid sequence of Figure 11 (Sequence ID Numbers 35 and 36) from glutamine, number 24 to glutamic acid, number 524, joined to an immunoglobulin heavy chain constant region domain selected from the group consisting of C_H1, C_H2, C_H3 and C_H4 joined to an immunoglobulin hinge region;

introducing into said cultured rodent myeloma cell a second DNA construct comprising a mouse V_K promoter operatively linked to a PDGF receptor signal sequence followed downstream of and in proper reading frame with a DNA sequence encoding the amino acid sequence of Figure 1 (Sequence ID Numbers 1 and 2) from isoleucine number 29, to lysine, number 531, joined to an immunoglobulin light chain constant region;

growing said cultured rodent myeloma cell in an appropriate growth medium under physiological conditions to allow the secretion of a PDGF receptor analog encoded by said first and second DNA sequences; and

isolating said PDGF receptor analog from said cultured myeloma cell.

26. A method for determining the presence of PDGF or an isoform thereof in a biological sample comprising the steps of:

incubating a polypeptide comprising a PDGF receptor analog joined to a dimerizing protein with a biological sample suspected of containing PDGF or an isoform thereof under conditions that allow the formation of receptor/ligand complexes; and

detecting the presence of receptor/ligand complexes, and therefrom determining the presence of human PDGF or an isoform thereof.

27. The method according to claim 26 wherein said biological sample is selected from the group consisting of blood, urine, plasma, serum, platelet and other cell lysates, platelet releasates, cell suspensions, cell-conditioned culture media, and chemically or physically separated portions thereof.

28. A method for purifying PDGF or an isoform thereof from a sample, comprising:

immobilizing a polypeptide comprising a PDGF receptor analog fused to a dimerizing protein on a substrate;

contacting a sample comprising PDGF or an isoform thereof with the immobilized polypeptide under conditions such that the PDGF or isoform thereof binds to the polypeptide; and

eluting the PDGF or isoform thereof from the polypeptide.

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